ABSTRACT OF THE DISCLOSURE

The method of the invention provides novel compounds, termed acid-labile
isotope-coded extractants (ALICE), for quantitative mass spectrometric analysis of
protein mixtures. The compounds contain a thiol-reactive group that is used to
capture cysteine-containing peptides from all peptide mixtures, an acid-labile linker,
and a non-biological polymer. One of the two acid-labile linkers is isotopically labeled
and therefore enables the direct quantitation of peptides/proteins through mass
spectrometric analysis. Because no functional proteins are required to capture
peptides, a higher percentage of organic solvent can be used to solubilize the peptides,
particularly hydrophobic peptides, through the binding, washing and eluting steps, thus
permitting much better recovery of peptides. Moreover, since the peptides are
covalently linked to the non-biological polymer (ALICE), more stringent washing is
allowed in order to completely remove non-specifically bound species. Finally, peptides
captured by ALICE are readily eluted from the polymer support under mild acidic
condition with high yield and permit the direct down stream mass spectrometric
analysis without any further sample manipulation. In combination with our novel dual
column two dimensional liquid chromatography- mass spectrometry (2D-LC-MS/MS)
design, the ALICE procedure proves to a general approach for quantitative mass
spectrometric analysis of protein mixtures with better dynamic range and sensitivity.